



The Association of Surgeons in Training

Group-A ($p > 0.039$) but also the overall survival ($p > 0.032$). Complete Surgical-clearance of tumour was achieved at a much higher significant rate in the Group-A ($p < 0.032$) which would constitute a cornerstone in improving survival. Side-effects for 131I-MIBG included toxicities in different patterns, however, complications were generally tolerated and non-fatal.

EXPLOITING WARBURG'S EFFECT FOR CLINICAL GAIN: PDK-3 IS A POTENTIAL TARGET FOR MITOCHONDRIAL MODULATION IN COLORECTAL CANCER (CRC)

S. Yeluri^{1,2}, B. Madhok^{1,2}, P. Prasad², M.J. Alemkunnappuzha², H.L. Thorpe³, S.L. Perry¹, T.A. Hughes¹, K.R. Prasad², P. Quirke¹, D.G. Jayne^{1,2}. ¹Leeds Institute of Molecular Medicine, University of Leeds; ²St. James's University Hospital, Leeds; ³Clinical Trials Research Unit, University of Leeds

Introduction: Cancers preference for glycolysis, with down-regulation of mitochondrial respiration, also known as the 'Warburg effect', provides a unique cancer target by modulation of mitochondrial respiration. We have examined the key regulators of glycolysis and mitochondrial respiration in CRC, to investigate its influence on outcome, and identify novel targets for anti-cancer therapy.

Methods: Antibody specificity was confirmed by western blotting. Tissue micro-arrays incorporating 280 CRCs were constructed and probed by immunohistochemistry for markers of glycolysis (HIF1 α , LDH5), and oxidative phosphorylation (PDK isoforms 1–4, PDC subunits E1 α , E2). Expression levels were scored semi-quantitatively, and compared to clinicopathological and 5-year survival data.

Results: Poorly differentiated tumours demonstrated significantly higher HIF1 α , and lower PDC-E1 α expression ($p < 0.05$). High HIF1 α , LDH5 and PDK1 expression was associated with high Dukes' stage ($p < 0.05$). High PDK3 ($p = 0.022$, HR = 1.92, 95% CI: 1.1, 3.36), and low PDC-E1 α ($p = 0.022$, HR = 1.60, 95% CI: 1.1, 2.4) expression were independent predictors of poor 5-year disease free survival, as were glycolytic markers- high HIF1 α ($p = 0.006$, HR = 2.11, 95% CI: 1.24, 3.58), and LDH5 ($p = 0.041$, HR = 1.57, 95% CI: 1.02, 2.41).

Conclusion: CRCs demonstrating Warburg's effect display aggressive biology, and are associated with significantly worse survival. The PDH/PDK system plays an important role in regulating Warburg's effect, with PDK3 an attractive anti-cancer target.

LIVER ISCHAEMIC PRECONDITIONING REDUCES LIVER ISCHAEMIA REPERFUSION INJURY ACTING THROUGH NITRIC OXIDE SYNTHASE INDEPENDENT OF HAEM OXYGENASE-1

G. Datta, B. Ramesh, B.J. Fuller, B.R. Davidson. Royal Free Hospital and Medical School, London, UK

Introduction: Ischaemia reperfusion injury (IRI) is a major cause of morbidity in liver transplantation. Haem oxygenase-1 (HO-1) and endothelial nitric oxide (NO) are protective mediators. This study sought examined the role of eNOS and HO-1 using a robust eNOS knockout model of ischaemic preconditioning rather than pharmacological agents which are nonspecific.

Methods: A murine model of partial hepatic ischaemia (45 min)/reperfusion (2 hr or 24 hr) was used. Groups: sham laparotomy; ischaemia reperfusion (IR) only; IPC with IR in both wild type (C57BL6) and eNOS knockout mice. Endpoints: Histology, sALT, Western Blot (eNOS, phospho-eNOS, HO-1) and RT-PCR (HO-1).

Results: IR resulted in IRI reflected in deranged ALT and histology. This injury was worse in knockouts than wild types. IPC reduced liver injury in wild types but this protection was abrogated in knockouts. IRI was associated with higher eNOS expression. HO-1 protein was not detected in any group, but HO-1 mRNA levels were seen in both wild type and knockouts after 2 hr reperfusion. HO-1 protein was detected in IPC and IR groups after 24 hr.

Conclusions: eNOS is a protective mediator of IPC in liver IRI. HO-1 expression is increased in the later stages of IPC and IRI and is not dependent on eNOS.

GENETICS AND SURGICAL OUTCOME: ARE THE TNF α PROMOTER POLYMORPHISMS -238A/G AND -308A/G IMPORTANT?

Fraser Welsh. University College London

Background: Ability to predict poor outcome after major surgery is clearly advantageous as treatment can be targeted accordingly. Excessive inflammatory response to surgery has been implicated in determining poor outcome. Recent studies have focused on the role of inflammatory cytokines; among the most significant is TNF α . Several functional polymorphisms have been identified in the TNF α gene. We examined the effect of major abdominal surgery on TNF α expression and examine the relevance of the TNF α -308A/G and -238A/G polymorphisms to surgery-induced inflammatory responses and outcome.

Methods: Blood was obtained from patients before and 24 hours after laparotomy for colorectal cancer. Genotypes for the -308A/G and -238A/G polymorphisms determined from DNA by PCR and restriction enzyme digestion. Gene transcription levels determined from RNA by RT-PCR. Plasma TNF α levels were determined by ELISA. Length of hospital stay and ITU stay determined from patients' notes.

Results and Conclusions: Colorectal surgery did not significantly alter TNF α transcription at 24 hours ($p = 0.36$) and did not significantly increase TNF α plasma levels ($p = 0.28$). The -238A/G or -308A/G polymorphisms did not significantly change transcription or plasma levels. Lengths of hospital stay were unaffected by genotype. Possession of a -238A allele increased the likelihood of an ITU stay post-operation ($p = 0.04$).

POOR NUTRITIONAL INTAKE IN ACUTE FRACTURED NECK OF FEMUR ADMISSION-IS THIS WELL DESCRIBED CLINICAL PROBLEM STILL UNDER MANAGED?

Peter J. Dacombe, Rhys G.E. Clement, James Woodard, Opinder Sahota. University of Nottingham, Division of Orthopaedic and Accident Surgery

Background: Fractured neck of femurs cause substantial morbidity, mortality and a huge financial burden to the NHS. Nutritional care, included in intercollegiate management guidelines, is too often overlooked in clinical practice.

Study Aim: To evaluate protein and energy intake of acute fractured neck of femur patients depending on admission MMSE, and compare these to department of health targets. Method: 40 fractured neck of femur admissions, recruited between December 08-March 09, were put into three groups depending on admission MMSE. Nutrition screening information (mid-arm circumference, grip strength, MUST score) was recorded, kcal and protein intake were calculated for a three day period.